The three-dimensional structure of lipoamide dehydrogenase from Azotobacter venelandii.

Schierbeek, Abraham Johan

5.4 Summary

The phased translation function is a simple and efficient algorithm that exploits prior phase information to solve the translation part of the molecular replacement problem. The prior phase information comes from isomorphous replacement in the cases we have tested; with the addition of even weak phase information, difficult translation problems become straightforward. We anticipate that this procedure would also be effective if the phase information came from a partial molecular replacement model, for example, a protein model omitting a flexible domain, or one member of a complex of two proteins.

Because the phased translation function is computed as a Fourier transform, it is quite efficient to evaluate. This efficiency, coupled with the relatively low sensitivity to errors in the orientation of the model, implies that fairly extensive 6-dimensional molecular replacement searches can be performed. Searches of the orientational parameters could be centered on peaks in the rotation function, but even a full 6-dimensional search could be contemplated. However, if the boundaries of a single molecule are visible, the domain rotation function of Colman et al. (1976b) probably gives a more efficient method of exploiting prior phase information to solve the rotation problem.

It is notoriously difficult to be convinced that molecular replacement is failing. Many parameters can be varied in the attempt to obtain a clear result. There is a strong incentive to continue because, when successful, molecular replacement requires much less work than isomorphous replacement. Our experience suggest that an entire structure determination by isomorphous replacement is not the only alternative. A single poor derivative might well provide all the extra information that is needed.

Acknowledgements

We thank Professor Wim G.J. Hol for his encouragement of this work. A.K. Muir pointed out the analogy between the phased translation function and the TRADIR procedure of P.T. Beurskens and co-workers.